CORONARY INTERVENTIONS IN THE ELDERLY

Jan Kaehler, Thomas Meinertz, Christian W Hamm

Heart 2006;**92**:1167–1171. doi: 10.1136/hrt.2005.071266

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Cardiovascular disease (CVD) is the leading cause of morbidity, mortality, and reduced quality of life in western cultures. Elderly patients, usually defined as those aged 65 years or above, are particularly affected; since they are the fastest growing segment of the population, the absolute prevalence of CVD will therefore increase further. Among cardiovascular diseases, coronary artery disease is—by quantity and quality—the most prominent one, a fact that emphasises the relevance of coronary interventions in these patients.

PERCUTANEOUS CORONARY INTERVENTION

With regard to percutaneous coronary intervention (PCI), many studies of the pre-stent era had rather disappointing results for elderly patients, lower success rates and frequent complications being the most prominent problems. In the meantime, because of improvements in interventional techniques, particularly the routine use of stents, outcomes have improved continuously while complications have decreased. A particularly striking example of this phenomenon are studies with recruitment periods lasting several years, in which significant improvements over time could be observed even within the individual trials.

However, since most interventional studies focus on patients aged 50–65 years, scientific evidence regarding the interventional treatment of the elderly is not as good as for younger patients. For this and other reasons, many physicians are still reluctant to suggest any invasive measure for elderly patients with known or suspected coronary artery disease.

An important insight from recent studies is the heterogeneity of risk observed for elderly patients. While peri-interventional mortality in elective PCI may be as low as 1% in the absence of risk factors, mortality increases exponentially in emergency situations involving multi-morbid patients, rising to more than 20%.

The treatment of the elderly in urgent settings is complicated by several problems: the elderly more often present with acute coronary syndromes, have longer intervals from the onset of symptoms to presentation, frequently complain of atypical symptoms, and frequently present with non-diagnostic ECGs. All these factors delay an appropriate treatment as compared to younger patients, in which the average lag between first symptoms and treatment is already far from ideal.

With regard to elective procedures, elderly patients are less frequently referred for angiography or PCI than younger patients, probably due to the perception that the risk-benefit relationship is not very attractive, and to adherence to the principle of ''primum non nocere'' (first do no harm).[1] This attitude might indirectly explain the frequent finding that the elderly who finally receive revascularisation appear to derive relatively more benefit from coronary interventions than younger patients.

This article will address issues that are particularly important in the invasive treatment of elderly patients with coronary artery disease, emphasising the indications and contraindications for interventional revascularisation.

PCI FOR STABLE ANGINA

The indication for PCI in patients with stable angina is particularly challenging since it is for symptomatic relief and therefore competes with medical treatment that may be sufficient for elderly patients with very limited physical activity. Therefore, a thorough evaluation of any factors potentially complicating PCI is of the utmost importance.

The underlying risk factor for all elderly patients—age—is statistically difficult to separate from risk factors that increase with age such as the severity and extent of coronary artery disease, or the presence of heart failure or diabetes.[2] Even in prospective studies such as the TIME (Trial of Invasive versus Medical therapy in Elderly patients) trial, the effect of age and of co-morbidities could not be statistically separated with certainty. Combining the data of recent studies, an age of 85 years without any other co-morbidities is probably associated with a two- to threefold increased procedure-related mortality, compared to average aged patients, as documented in a

See end of article for authors' affiliations

Correspondence to:
Dr Jan Kaehler, Department of Cardiology, University Hospital Eppendorf, Martinistr. 52, 20246 Hamburg, Germany;
kaehler@uke.uni-hamburg.de

Table 1 Multivariate predictors of octogenarian mortality

	Odds ratio	95% CI	p Value
Shock	5.4	3.3 to 8.8	<0.001
Acute MI	3.2	2.3 to 4-4	<0.001
LVEF <35%	2.9	2.1 to 3.9	<0.001
Renal insufficiency	2.8	2.0 to 3.8	<0.001
First PTCA	2.3	1.7 to 3.3	<0.001
Age >85 years	2.1	1.5 to 2.7	<0.001
Diabetes mellitus	1.5	1.1 to 2.0	0.005

Adapted from Batchelor *et al*.[2]
CI, confidence interval; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty

large database from North America (table 1).[2] Taking into account the contemporary risks in an average-aged population, this translates into a rate of in-hospital mortality of less than 2%.

Further risk factors for elderly patients undergoing PCI are similar to those found in younger patients, but are more frequent: previous myocardial infarction, previous coronary revascularisation, reduced left ventricular ejection fraction, cerebrovascular disease, peripheral vascular disease, renal insufficiency, and diabetes mellitus.[2]

It therefore is of paramount importance to thoroughly evaluate elderly patients with symptomatic coronary artery disease for risk factors and potential co-morbidities such as peripheral vascular problems or pre-existing renal failure. Once the risk factors are known and the resulting risk of an intervention has been estimated, the investigator should have a plan for how to proceed in the case of complications—for example, how far resuscitation should be pursued. All relevant aspects then have to be discussed with the patient, ascertaining that PCI is the approach to symptom relief that reflects the patient's preferences.

The randomised TIME trial demonstrated that four-year outcomes in elderly patients with stable angina, average age 80 years, are similar in regard to symptoms, quality of life, and death or non-fatal infarction with invasive versus optimised medical strategies. The invasive approach carried an increased early peri-interventional risk, while medical management posed an almost 50% chance of later hospitalisation and revascularisation (fig 1).[3]

According to these data, the choice has to be made between: (1) a watch-and-wait approach with intensified medical treatment, with an initial lower risk but a 50% probability for subsequent interventions; and (2) an early invasive strategy with an up-front higher risk, but swift gains in quality of life and a reduced downstream risk for intervention in urgent or emergency situations. The pros and cons of these two alternatives have to be weighed against the specific risk profile, so that ultimately an individual approach can be outlined for every patient, probably more and more often being early invasive.

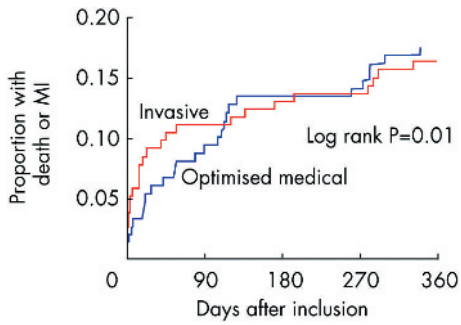

Figure 1 Kaplan–Meier plot of time to death or non-fatal myocardial infarction in elderly patients of the TIME trial treated with invasive or optimised medical treatment. The initially increased risk in interventionally treated patients is balanced during later follow-up. Adapted from Pfisterer *et al*.[3]

The revascularisation of all diseased coronary segments—complete myocardial revascularisation—has potential long-term benefits with regard to repeat interventions and life expectancy, but is more complex and may increase in-hospital events. While the beneficial effect on life expectancy is proven for average aged patients undergoing PCI, for elderly patients data are sparse. However, for elderly patients undergoing coronary artery bypass graft surgery (CABG), two studies involving up to 5000 patients found that complete revascularisation was associated with a better prognosis.

As PCI in the elderly is predominantly symptom-oriented, it appears reasonable to focus on treating the culprit lesion in the majority of patients. Only in ''young'' elderly patients, with excellent health apart from the coronaries, should an attempt of complete revascularisation be considered.

With regard to the use of drug eluting stents (DES), there has been vigorous discussion as to whether or not elderly patients should receive DES. As reliable data are lacking, the arguments can be summarised as follows. There is no reason to withhold DES from the elderly since the time frame of DES-advantage is months, a period in which the limited life expectancy of most elderly patients is not relevant. In contrast, since complication rates in elective PCI are still marginally higher in the elderly, one would be particularly interested in avoiding reinterventions—an effective tool for achieving this being the use of DES. Prolonged co-medication with aspirin and clopidogrel, potentially increasing bleeding complications, should not significantly outweigh these potential benefits.

QUALITY OF LIFE FOLLOWING PCI IN ELDERLY PATIENTS WITH STABLE ANGINA

Since life expectancy decreases with age, the main reason for elderly patients undergoing elective PCI is for improving quality of life. Patients themselves usually state that they are interested in symptomatic improvement, while length of life is only of marginal interest. Although specific sociocultural aspects come into play when quality of life is measured in elderly patients, quality of life can be measured reproducibly and should be the major outcome measure for elective PCI.

Although only a few studies have addressed the issue of quality of life following PCI in elderly patients, their rather homogenous finding was that the benefit for elderly or even octogenarian patients was equal or higher than that of younger patients.[1 4] Technical conditions for PCI are not as good in elderly patients because peripheral and coronary vessels are more severely diseased, and interventional success rates also tend to be less satisfactory. Therefore, the most likely explanation for this phenomenon is that elderly patients are referred rather late with more severe symptoms than younger patients are, so that interventions are relatively more effective in the elderly. As complications are infrequent in those elderly patients with no or few risk factors, one approach could be to offer PCI more liberally to selected elderly patients with stable angina.

PCI VERSUS CABG FOR STABLE ANGINA

Outcomes of cardiac surgery have improved significantly over recent decades; in particular, elderly patients with no or minor risk factors can be operated on with good results with an in-hospital mortality of less than 4%. While modern surgical techniques such as minimal invasive CABG or off-pump bypass surgery may reduce complications, frequent co-morbidities in the elderly can be problematic for surgical revascularisation, particularly chronic obstructive pulmonary disease and cerebrovascular disease. Further, when CABG is combined with valve surgery, the perioperative risk increases, even in patients with no risk factors, up to a mortality of 18% in patients aged ⩾ 80 years.[5 6]

Data directly comparing PCI with CABG are sparse. In a large Canadian study, 6200 patients aged 70 years or above with stable or unstable angina were treated with bypass surgery, PCI or medication and followed up for four years. Although selection bias could not be completely eliminated, both surgically and interventionally treated patients had far better survival than those treated medically. In 15 390 "control" patients < 70 years of age, four-year adjusted actuarial survival rates for CABG, PCI and medical treatment were 95.0%, 93.8% and 90.5%, respectively. In 5200 patients aged 70–79 years, respective survival rates were 87.3%, 83.9% and 79.1%. In 980 patients ⩾ 80 years of age, survival was 77.4% for CABG, 71.6% for PCI and 60.3% for medical treatment. Absolute risk differences in comparison to medical treatment for CABG (17.0%) and PCI (11.3%) were greater for patients ⩾ 80 years of age than for younger patients. As previously discussed for quality of life issues, the greater effect in the oldest patients was probably due to the overrepresentation of highly symptomatic patients in this group, supporting the observation that particularly very old patients are relatively undertreated.[7]

PCI IN NON-ST-ELEVATION ACUTE CORONARY SYNDROMES

In several registries of patients with non-ST-elevation acute coronary syndromes, elderly patients received heparin, β blockers and statins significantly less frequently than younger patients. Similarly, older patients had significantly lower rates of angiography and revascularisation, reflecting a relative underuse of medical resources in these patients. Both the proportion of female patients and mortality increase in higher-aged cohorts—for example, six-month mortality increases from 1.7% in the age group < 60 years to 15% in those aged 80 years or above; in the same groups, rates of coronary intervention were 19% and 3%, respectively.[8]

Contributing to the a priori worse prognosis of elderly patients is the more severe disease status—elderly patients more frequently present with ST segment depression, high TIMI (Thrombolysis in Myocardial Infarction) risk score, and troponin positivity.

In regard to PCI, with the exception of one early trial (VANQWISH), in most studies elderly subgroups treated by early PCI had outcomes as favourable as those treated with medical or delayed interventional therapies (fig 2).[9] Data from a subgroup analysis of the TACTICS-TIMI 18 trial—in which patients were randomised to an early invasive or conservative strategy—suggest that, with regard to six-month mortality, the early invasive strategy yielded an absolute risk reduction from 14% to 9%, and a relative reduction of death by 39% in elderly patients. This was significantly more than in younger patients, while the risk for stroke was not higher, although major bleeding increased from 7% to 17%.[10]

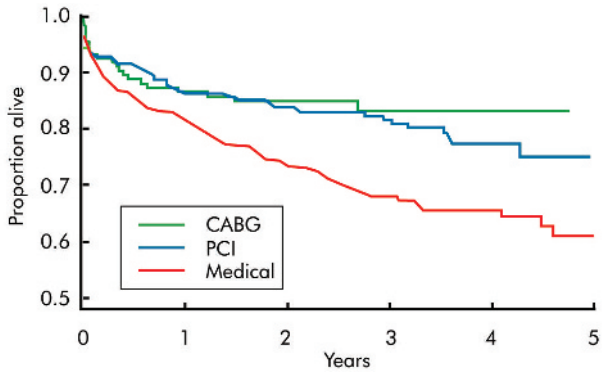

Figure 2 Kaplan–Meier plot of survival of patients aged 80 or above. Both patients treated with percutaneous coronary intervention (PCI) or surgical bypass grafting (CABG) had significantly better survival than patients treated medically. Adapted from Graham *et al*.[7]

In conclusion, despite an increased risk for bleeding and a good chance of being confronted with a complex coronary situation, there is no reason to withhold angiography and PCI from elderly patients with non-ST elevation acute coronary syndrome.

PCI IN ST ELEVATION MYOCARDIAL INFARCTION

Age is a strong determinant of short- and long-term prognosis in patients with acute myocardial infarction; in the era before reperfusion elderly patients ⩾ 65 years of age had one-month and one-year mortality rates of 30% and 75%, respectively. Despite contemporary interventional techniques, mortality exponentially increases in patients after 65 years of age; in the CADILLAC (Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications) trial one-year mortality increased sevenfold from 1.6% to 11% in patients < 65 years versus those ⩾ 75 years of age.[11] To a large extent this is due to the fact that patients for elective PCI can be selected according to their risk profile, but one has to cope with the usually numerous risk factors that are present once a patient is admitted with acute myocardial infarction. However, despite the a priori worse prognosis in elderly patients, success rates of PCI and rates of TIMI-3 flow achieved are comparable to those in younger patients, provided modern antithrombotic drugs are used.

Women with ST elevation myocardial infarction, who outnumber men in the age group 80 years and above, benefit particularly from PCI, as shown in the Cooperative Cardiovascular Project (CCP) experience and the NRMI-2 registry with 632 elderly patients. In a subgroup of 20 700 patients of the CCP trial, the adjusted 30-day mortality in woman could be reduced from 15.4% with thrombolysis to 10.4% with PCI; the effect in men was less pronounced, from 10.5% to 8.6%. In both groups, these advantages of PCI were preserved over a one-year follow-up period.

Subgroup analyses and one study with elderly patients suggest that PCI is safe and superior to thrombolysis with accelerated tissue-type plasminogen activator or streptokinase, as in average-aged patients, when transfer time is below three hours.[12]

In a pooled analysis of studies comparing PCI with thrombolytic therapy (n = 2534), in-hospital mortality of patients ⩽ 70 years could be reduced from 5% with

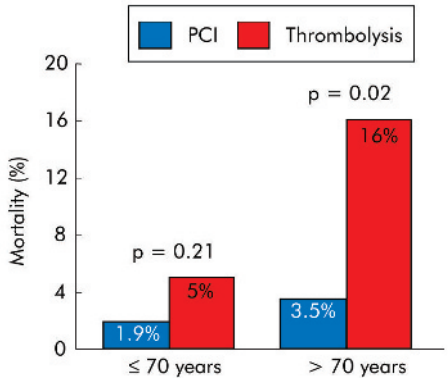

Figure 3 Comparison of age-related hospital mortality pooled from the PAMI, Mayo, and Netherlands randomised trials comparing percutaneous coronary intervention (PCI) with thrombolytic treatment (n = 2534). In particular, patients aged > 70 years benefited from PCI. Adapted from ONeill *et al*.[13]

thrombolysis to 1.9% with PCI, while mortality of patients > 70 years was reduced from 16% with thrombolysis to 3.5% with PCI (fig 3). This trend that patients with the highest risk benefit most from coronary interventions has also been frequently documented in other studies.[13]

Although potential tradeoffs between risks, particularly bleeding and stroke, cannot be assessed accurately for elderly patients, the trend in these studies indicates that bleeding complications are relatively high with both methods. While more strokes occurred with thrombolysis, with a frequency of 3.3%, only 1.0% of patients undergoing PCI suffered from a stroke. In contrast, more major bleeding episodes were documented with PCI (8.8% *v* 5.6%).

Even in a community-based approach, in a subgroup analysis of the GRACE study with 1130 patients 70 years or older, adjusted in-hospital mortality was lower with PCI versus thrombolysis while the rate of reinfarction was reduced from 6% to 1%. In contrast, the risk for stroke or major bleeding was only insignificantly reduced in PCI versus thrombolysis (table 2).[14]

CONCOMITANT TREATMENT

Clinical efficacy of antithrombotic treatments is rarely reported for elderly patients. So far, only data for aspirin, clopidogrel and glycoprotein IIb/IIIa antagonists are available, showing that these substances are effective in elderly patients. In a study with 1400 patients aged above 80 years using contemporary interventional techniques, it could be demonstrated for several glycoprotein IIb/IIIa antagonists that clinical efficacy was comparable to that in younger patients. While bleeding was more frequent in elderly patients, transfusion rate was not significantly elevated and no cases of intracranial haemorrhage were observed.[15] However, in several other studies, the risk of bleeding with glycoprotein IIb/IIIa antagonists was reported to be higher in elderly patients, and consecutive transfusion rates were higher as well. For clopidogrel, the CURE study also demonstrated efficacy in elderly patients, but the effect was less pronounced than in younger patients.

Therefore, mainly two aspects of antithrombotic treatment in elderly patients have to be considered: (1) increased likelihood of complications due to the fragile and bleeding-prone vessels in these patients, particularly at the vascular access site; and (2) frequently reduced kidney function leading to overdosing of substances such as low molecular weight heparins. Both mechanisms contribute to the increased risk of bleeding in elderly patients and careful dosage of antithrombotic medication is mandatory in these patients.

Coronary interventions in the elderly: key points

- Risk factors associated with higher age rather than age itself increase the risk of percutaneous coronary intervention
- In selected elderly patients with stable angina, peri-interventional risk can be as low as 1%
- Elderly patients have a notably increased risk of acute ischaemic syndromes
- Particularly elderly high-risk patients with acute ischaemic syndromes benefit from early percutaneous coronary intervention
- Efficacy of antithrombotic treatment in the elderly is comparable to that in younger patients while bleeding is more frequent

TREATMENT STRATEGY IN ELDERLY PATIENTS

The major difference with elderly patients undergoing PCI is that their prognosis—a priori and following PCI—is far more variable than that of younger patients. This fact makes it essential to perform a comprehensive evaluation before revascularisation in all elderly patients. Furthermore, patients themselves have to be questioned regarding their expectations that again are far more variable than in younger patients.

Therefore, in summary, the challenge of working with elderly candidates for PCI is that the patients, the indications and the procedures have to be selected particularly carefully. The following criteria may be used for decision-making:

- In patients with stable angina, patients with a low peri-interventional risk can be easily identified by their medical history and an evaluation for signs of heart failure, peripheral vascular problems and renal function. In most

Table 2 In-hospital outcomes for primary percutaneous coronary intervention (PCI) versus thrombolysis in acute myocardial infarction in elderly patients

	Primary PCI n = 365 n (%)	Thrombolysis n = 769 n (%)	Adjusted odds ratio	95% CI	p Value
All-cause mortality	49 (13.5)	113 (14.8)	0.62	0.39 to 0.96	0.03
Reinfarction	4 (1.1)	44 (5.7)	0.15	0.05 to 0.44	<0.001
Cardiogenic shock	41 (11.3)	88 (11.6)	0.71	0.43 to 1.16	0.82
Major bleeding	31 (8.6)	45 (5.9)	1.17	0.69 to 1.99	0.56
Stroke	4 (1.1)	21 (21.8)	0.42	0.13 to 1.34	0.14

Adapted from Mehta *et al*.[14]

of the low risk patients, a substantial improvement of symptoms can be achieved by PCI of the culprit lesion, and even complete revascularisation may be considered.

- In patients with stable angina and an intermediate or high risk according to risk stratification, a decision has to be made when intensified medical treatment is without satisfactory effect. However, the potential benefit of PCI has to be weighed against the elevated risk for peri-interventional complications.
- In acute coronary syndrome settings, in urgent situations, risks are generally high for elderly patients. However, in these situations, the potential benefit of PCI increases towards those patients of the highest risk groups. Therefore, when the patient appears healthy enough to leave hospital and return to a meaningful life at home, one has to weigh the elevated risks against the increased potential benefit in this high-risk group. However, reperfusion therapy by PCI is the preferred strategy, both in patients with or without ST elevation.

Authors' affiliations

J Kaehler, T Meinertz, Department of Cardiology, University Hospital Eppendorf, Hamburg, Germany
C W Hamm, Department of Cardiology, Kerckhoff Heart Center, Bad Nauheim, Germany

In compliance with EBAC/EACCME guidelines, all authors participating in Education in *Heart* have disclosed potential conflicts of interest that might cause a bias in the article

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